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TOR: a new orphan receptor expressed in the thymus that can modulate retinoid and thyroid hormone signals.

Ortiz MA, Piedrafita FJ, Pfahl M, Maki R
Mol Endocrinol 1995 Dec 9:1679-91

BROWSE : [Mol Endocrinol](#) • [Volume 9](#) • [Issue 12](#)
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Abstract

Vitamin A and other fat-soluble hormones and vitamins have important roles as modulators of essential biological processes such as homeostasis, development, differentiation, and oncogenesis and also as regulators of the immune system. The active form of vitamin A, retinoic acid, as well as vitamin D3 and thyroid hormones exert their actions by binding to specific nuclear receptors that represent one subfamily of the steroid/thyroid hormone receptor superfamily. To identify new members of the retinoid/thyroid hormone receptor subfamily that could play a role in the immune system, a screening of a T cell cDNA library was performed using a retinoid X receptor probe. A clone was isolated encoding a novel nuclear receptor expressed mainly in the thymus and T cell lines. This new receptor, TOR (thymus orphan receptor), is most closely related in both its DNA-binding domain and ligand-binding domain, 90% and 53%, respectively, to ROR alpha/RZR alpha and clusters with these two receptors and RZR beta in a phylogenetic tree, when both the DNA-binding domain and the ligand-binding domain sequences of nuclear receptors are compared. Thus, TOR is part of a subgroup of receptors, one of which has recently been reported to be activated by melatonin. TOR binds specifically to a direct repeat of the half-site sequence 5'-AGGTCA-3' with a four- or five-nucleotide spacer, DNA sequences that also serve as binding sites for thyroid hormone (TR), and retinoic acid receptors (RAR). In transient transfection experiments TOR does not activate a reporter gene carrying these sequences in the absence or the presence of any known nuclear receptor ligands. TOR, however, is able to repress TR and RAR activity on DR-4-TREs or DR-5-RAREs, respectively. Therefore, our data suggest that TOR, similar to COUP-TF, can negatively regulate retinoic acid and thyroid hormone signals. However, the response elements recognized by TOR and COUP-TF differ as do the expression patterns of these receptors. Thus, one important role of TOR could be to modulate retinoid and thyroid hormone signals in the thymus.

MeSH

-continued

(B) TYPE: nucleic acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: cDNA
(A) DESCRIPTION: hIL-4/R121I

(iii) HYPOTHETICAL: no

(iv) ANTI-SENSE: no

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 8:

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| Met Gly Leu Thr Ser Gln Leu Leu Pro Pro Leu Phe Phe Leu Leu | |
| 1 5 10 15 | |
| GCA TGT GCC GGC AAC TTT GTC CAC GGA CAC AAG TGC GAT ATC ACC | 90 |
| Ala Cys Ala Gly Asn Phe Val His Gly His Lys Cys Asp Ile Thr | |
| 20 25 30 | |
| TTA CAG GAG ATC ATC AAA ACT TTG AAC AGC CTC ACA GAG CAG AAG | 135 |
| Leu Gln Glu Ile Ile Lys Thr Leu Asn Ser Leu Thr Glu Gln Lys | |
| 35 40 45 | |
| ACT CTG TGC ACC GAG TTG ACC GTA ACA GAC ATC TTT GCT GCC TCC | 180 |
| Thr Leu Cys Thr Glu Leu Thr Val Thr Asp Ile Phe Ala Ala Ser | |
| 50 55 60 | |
| AAG AAC ACA ACT GAG AAG GAA ACC TTC TGC AGG GCT GCG ACT GTG | 225 |
| Lys Asn Thr Thr Glu Lys Glu Thr Phe Cys Arg Ala Ala Thr Val | |
| 65 70 75 | |
| CTC CGG CAG TTC TAC AGC CAC CAT GAG AAG GAC ACT CGC TGC CTG | 270 |
| Leu Arg Gln Phe Tyr Ser His His Glu Lys Asp Thr Arg Cys Leu | |
| 80 85 90 | |
| GGT GCG ACT GCA CAG CAG TTC CAC AGG CAC AAG CAG CTG ATC CGA | 315 |
| Gly Ala Thr Ala Gln Gln Phe His Arg His Lys Gln Leu Ile Arg | |
| 95 100 105 | |
| TTC CTG AAA CGG CTC GAC AGG AAC CTC TGG GGC CTG GCG GGC TTG | 360 |
| Phe Leu Lys Arg Leu Asp Arg Asn Leu Trp Gly Leu Ala Gly Leu | |
| 110 115 120 | |
| AAT TCC TGT CCT GTG AAG GAA GCC AAC CAG AGT ACG TTG GAA AAC | 405 |
| Asn Ser Cys Pro Val Lys Glu Ala Asn Gln Ser Thr Leu Glu Asn | |
| 125 130 135 | |
| TTC TTG GAA AGG CTA AAG ACG ATC ATG ATA GAG AAA TAT TCA AAG | 450 |
| Phe Leu Glu Arg Leu Lys Thr Ile Met Ile Glu Lys Tyr Ser Lys | |
| 140 145 150 | |
| TGT TCG AGC TAG | 462 |
| Cys Ser Ser End | |
| 153 | |

(2) INFORMATION FOR SEQ ID NO: 9:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 462
(B) TYPE: nucleic acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: cDNA
(A) DESCRIPTION: hIL-4/R121K

(iii) HYPOTHETICAL: no

(iv) ANTI-SENSE: no

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 9:

| | |
|---|----|
| ATG GGT CTC ACC TCC GAA CTG CTT CCC CCT CTG TTC TTC CTG CTA | 45 |
| Met Gly Leu Thr Ser Gln Leu Leu Pro Pro Leu Phe Phe Leu Leu | |
| 1 5 10 15 | |
| GCA TGT GCC GGC AAC TTT GTC CAC GGA CAC AAG TGC GAT ATC ACC | 90 |